PABST PATENT GROUP

Pabst Patent Group LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, GA 30361

Telephone (404) 879-2150
Telefax (404) 879-2160

information@pabstpatent.com
www.pabstpatent.com

TELEFAX

Date: January 31, 2005

Total pages: 26 (incl. cover sheet)

To: US PTO

Telephone:

Telefax: 703-872-9306

From: Patrea L. Pabst

Telephone: 404-879-2151

Telefax: 404-879-2160

Our Docket No. CP 101 CIP
Your Docket No.

Client/Matter No. 0085337/4

Please call (404) 879-2150 if you did not receive all of the pages, or if they are illegible.

MESSAGE:

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Saul Tzipori, Ramaswamy Balakrishnan and Arthur Donohue-Rolfe

Serial No.: 10/041,958 Art Unit: 1645

Filed: January 7, 2002 Examiner: Mark Navarro

For: *HUMAN NEUTRALIZING ANTIBODIES AGAINST HEMOLYTIC UREMIC SYNDROME*

Transmittal of Documents after Initial Filing, Fee Transmittal, Request for Oral Hearing, Reply to Examiner's Answer.

(45054170.1)
085337-00004

45054170_1.DOC

PTO/SB/21 (09-04)
Approved for use through 07/31/2005. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	10/041,958
Filing Date	January 7, 2002
First Named Inventor	Saul Tzipori
Art Unit	1645
Examiner Name	Mark Navarro
Attorney Docket Number	CP 101 CIP

ENCLOSURES *(Check all that apply)*

- [✓] Fee Transmittal Form
  - [ ] Fee Attached
- [✓] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- [ ] Proprietary Information
- [ ] Status Letter
- [✓] Other Enclosure(s) (please identify below):
  Request for Oral Hearing

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Pabst Patent Group LLP		
Signature			
Printed name	Patrea L. Pabst		
Date	January 31, 2005	Reg. No.	31,284

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name	Patrea L. Pabst	Date	January 31, 2005

PTO/SB/17 (12-04)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Effective on 12/08/2004.
Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL
For FY 2005

☑ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 500.00

Complete if Known	
Application Number	10/041,958
Filing Date	January 7, 2002
First Named Inventor	Saul Tzipori
Examiner Name	Mark Navorro
Art Unit	1645
Attorney Docket No.	CP 101 CIP

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit Card ☐ Money Order ☐ None ☐ Other (please identify): _____

☑ Deposit Account Deposit Account Number: 50-3129 Deposit Account Name: Pabst Patent Group LLP

For the above-identified deposit account, the Director is hereby authorized to: (check all that apply)

☑ Charge fee(s) indicated below ☐ Charge fee(s) indicated below, **except for the filing fee**

☑ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 ☑ Credit any overpayments

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

Application Type	FILING FEES Fee ($)	FILING FEES Small Entity Fee ($)	SEARCH FEES Fee ($)	SEARCH FEES Small Entity Fee ($)	EXAMINATION FEES Fee ($)	EXAMINATION FEES Small Entity Fee ($)	Fees Paid ($)
Utility	300	150	500	250	200	100	
Design	200	100	100	50	130	65	
Plant	200	100	300	150	160	80	
Reissue	300	150	500	250	600	300	
Provisional	200	100	0	0	0	0	

2. EXCESS CLAIM FEES

Fee Description	Fee ($)	Small Entity Fee ($)
Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent	50	25
Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent	200	100
Multiple dependent claims	360	180

Total Claims	Extra Claims	Fee ($)	Fee Paid ($)
11 - 20 or HP =	0	x -0.00	=00

HP = highest number of total claims paid for, if greater than 20

Indep. Claims	Extra Claims	Fee ($)	Fee Paid ($)
1 - 3 or HP =	0	x 0.00	=

HP = highest number of independent claims paid for, if greater than 3

Multiple Dependent Claims Fee ($)	Fee Paid ($)

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is $250 ($125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

Total Sheets	Extra Sheets	Number of each additional 50 or fraction thereof	Fee ($)	Fee Paid ($)
- 100 =	/ 50 =	(round up to a whole number)	x	=

4. OTHER FEE(S)

Fees Paid ($)

Non-English Specification, $130 fee (no small entity discount)

Other: Request for Oral Hearing (Small Entity) $500.00

SUBMITTED BY

Signature		Registration No. (Attorney/Agent) 31,284	Telephone (404) 879-2152
Name (Print/Type)	Patrea L. Pabst		Date January 31, 2005

RECEIVED
CENTRAL FAX CENTER
JAN 3 1 2005

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant:	Saul Tzipori, Ramaswamy Balakrishnan, and Arthur Donohue-Rolfe		
Serial No.:	10/041,958	Art Unit:	1645
Filed:	January 7, 2002	Examiner:	Mark Navarro
For:	*HUMAN NEUTRALIZING ANTIBODIES AGAINST HEMOLYTIC UREMIC SYNDROME*		

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY TO EXAMINER'S ANSWER

Sir:

This is a reply to the Examiner's Answer mailed November 30, 2004 in the above identified patent application. A request for Oral Hearing is enclosed along with the appropriate fee for a small entity. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

Appellants have appealed the rejection of claims 26-36 in the Office Action mailed April 16, 2004. A Notice of Appeal was filed on July 16, 2004. An Appeal Brief was filed September 14, 2004.

The issue presented on appeal is whether claims 26-36 are obvious under 35 U.S.C. § 103(a) over U.S. Patent No. 5,512,28 to Krivan *et al.* ("Krivan") and Perera, et al., J.

Clin.Microbiol. 26(10), 2127-2131 (1988) ("Perera") in view of WO 90/07861 by Queen *et al.* ("Queen") and Engelman *et al.*, Human Hybridomas and Monoclonal Antibodies, NY Plenum Press 1985 pp. 23-27 ("Engelman") and further in view of U.S. Patent No. 6,080,400 to Williams ("Williams").

Appellants affirm all arguments set forth in the Appeal Brief. The following remarks are submitted in response to the Examiner's Answer.

Response to Examiner's Answer

(a) Rejections Under 35 U.S.C. § 103

Claims 26-36 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,512,282 to Krivan *et al.* ("Krivan") and Perera *et al.* J. Clin. Microbiol. 26(10):2127-2131 (1988) ("Perera") in view of WO 90/07861 by Protein Design Labs, Inc ("Queen") and Engelman *et al.* "Human Hybridomas and Monoclonal Antibodies ed. Engleman, Foung, Larrick, Raubitschek (Plenum Press 1985) pp. 95-112 ("Engelman") and further in view of U.S. Patent No. 6,080,400 to Williams.

The examiner has improperly analyzed the prior art using hindsight to provide the motivation for one skilled in the art to select the claimed elements out of many different and in some cases contradictory lists of elements. Nothing in the cited art provides one skilled in the art with a reasonable expectation of success that, even if one did select the claimed elements.

When applying 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

"References relied upon to support a rejection under 35 USC 103 must provide an enabling disclosure, i.e., they must place the claimed invention in the possession of the public." *Application of Payne*, 606 F.2d 303, 314, 203 U.S.P.Q. 245 (C.C.P.A. 1979); *see Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 13 U.S.P.Q.2d 1301 (Fed. Cir. 1989). A publication that is insufficient as a matter of law to constitute an enabling reference may still be relied upon, but only for what it discloses. *See Reading & Bates Constr. Co. v. Baker Energy Resources Corp.*, 748 F.2d 645, 651-652, 223 U.S.P.Q. 1168 (Fed. Cir. 1984); *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569 (Fed. Cir. 1991).

"Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." *Gillette Co. v. S.C. Johnson & Sons, Inc.*, 919 F.2d 720, 724, 16 U.S.P.Q.2d 1923 (Fed. Cir. 1990); *see Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383, 231 U.S.P.Q. 81, 93 (Fed. Cir. 1986). "One cannot use hindsight reconstruction to pick and choose

among isolated disclosures on the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). The prior art must provide one of ordinary skill in the art with the motivation to make the proposed modifications needed to arrive at the claimed invention. *See In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987); *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). Furthermore, the prior art must provide one of ordinary skill in the art with the motivation "to combine pieces" to arrive at the claimed invention. *See Yamanouchi Pharmaceutical Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 56 USPQ2d 1641 (Fed. Cir. 2000). Claims for an invention are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims. *In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992). *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989). This is not possible when the claimed invention achieves more than what any or all of the prior art references allegedly suggest, expressly or by reasonable implication. Furthermore, In *In re Vaeck* (947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)), the Federal Circuit noted: "Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. ... Both the suggestion

and the reasonable expectation of success must be founded in the prior art, not in the appellant's disclosure." Here, the references do not teach one skilled in the art to select an antibody to a subunit of Stx2, in a therapeutically effective dosage, to treat or prevent HUS.

The Claimed Invention

The claimed invention is a composition of (1) human or humanized monoclonal antibodies (2) neutralizing Shiga like toxin II in vivo that (3) are reactive with a single subunit of the Shiga like toxin II (4) in an effective dosage to treat or prevent hemolytic uremic syndrome ("HUS")in a human (claim 26).

The appellants have asserted, and provided expert evidence that, one of skill in the art at the time this application was filed, would have been unable to determine that antibodies to a single subunit would be effective to treat or prevent HUS except by using an appropriate animal model, which appellants discovered was a neonatal gnotobiotic piglet infected with a human virulent strain of *E. coli.*

Even then, absent the model, one could not determine which subunit had to be neutralized for the antibodies to be effective in humans, much less what the appropriate dosage would be.

The Prior Art:

The examiner continues to cite to references that describe various pieces of what is claimed, or at least various pieces which can be modified to be the claimed elements, but never shows where the cited art provides either the motivation to select and modify as appellants have done nor why one of skill in the art would have a reasonable expectation that such a selection

would be effective. He has repeatedly used appellants own teachings to then pick and choose out of the cited art support for his rejection. This is not the legal test!

Williams

Williams does not disclose a monoclonal antibody to a subunit of Shiga like toxin II which causes severe illness in humans. Williams makes polyclonal antibodies to recombinant proteins expressed in birds. Col. 5, line 48 begins a discussion of the two Shiga like toxins ("SLT") produced in enteropathogenic *E. coli*. At col. 6, lines 18-29, it is noted that it is only VT1 (corresponding to SLT I) that is enzymatically activ and a toxin, and that VT2 (corresponding to the claimed SLTII) merely binds to a receptor. See especially col. 6, lines 51-55, which explicitly states that VT1 (SLTI) is required for toxicity. Col. 7, lines 1-22, indicates that while SLTII is important for toxicity, and antibodies can neutralize its activity, there is nothing that says this is the subunit that determines whether or not HUS develops with lethal consequences in infected humans. Col. 27, lines 53-60, state that it is preferred to administer antibody neutralizing both VT1 and VT2. In summary, there is no teaching that the SLTII is critical to pathogenicity and that neutralization of this subunit alone can limit HUS. Indeed, the teaching of the reference has a whole leads one to believe it is critical to neutralize the SLTI.

As the examiner has correctly noted, Williams does not disclose monoclonal antibodies. Williams is focused on polyclonal antibodies made in birds, especially antibody isolated from eggs, which is treated to reduce side effects associated with the bird proteins. See col. 27, line 61 to col. 28, line 24.

Williams defines a "therapeutic amount" at col. 14, lines 47-49, as "that amount of antitoxin required to neutralize the pathologic effects of *E. coli* toxin in a subject." There is no indication of what this actually constitutes, however, other than some very vague conjecture at col. 28, lines 44-58, which ranges from a single injection of less than 10 grams of impure protein up to less than 100 mg of pure protein. Even though Williams refers to data in mice, which appellants have shown are not predictive of HUS in human, Williams also recognizes the deficiencies of available animal models, noting that none of the available animal models "produce all the pathologies and symptoms of hemorrhagic colits, HUS, and TTP which occur in humans. Glomerular damage is noticeably absent." Col. 8, lines 26-31. Accordingly, Williams acknowledges that he has no model to predict an effective dosage to prevent HUS in humans, since he has no model that is predictive of HUS in humans.

Perera, et al.

Perera describes murine monoclonal antibodies prepared by immunization with formalinized or glutaraldehyde crosslinked toxin obtained from humans, calves or pigs (col. 2, page 2127) – it is therefore not even certain what toxin was actually used and what the antibodies react to (note statement col. 2, page 2129 "These findings suggest that the MAbs recognize conformation rather than sequence-determined epitopes." Col. 1, page 2130, suggests that the authors recognized that the protein crosslinking could have altered the structure of the native epitopes.. Antibodies demonstrated immunoreactivity with toxin in conventional ELISAs. Toxin subunits were separated using urea, which were then placed in the ELISAs. The authors

goal was not to make a therapeutic, but to provide a rapid diagnostic test (page 2127). There is no indication the antibodies (even if there was some teaching to humanize) would be effective in preventing or treating HUS, no suggestion that antibodies just to SLTII should be used as a therapeutic, and certainly nothing that indicates what a therapeutically effective amount. The only reference to role of the toxins (not the antibodies) in disease is found at col. 2, page 2130, "Epidemiological evidence strongly suggests that the SLTs of E. coli play a role in disease in both humans and animals (8, 10, 11, 17-19, and 24), although no direct proof for the involvement of SLTs in pathogenesis has yet been demonstrated." With respect to SLTII, the authors note at col. 1, page 2131, "Second, of teh SLT-II –producing E. coli strains tested, all high-level cytotoxin producers were detected by at least one of the MAbs to SLT-II. However, it should be emphasized that SLT-II-producing strains in the high-level category (>10^5 to 10^8 CD_{50}/ml of cytotoxin in bacterial sonic lysate) are actually producing both SLT-I and SLT-II (17). . . . Third, three of the strains that produced only SLT-II did not react in the colony ELISA with any of the neutralizing MAbs to SLT-II.... These three strains may produce SLTs more like the SLT-IIv-producing edema disease strains."

Krivan

Krivan has been discussed extensively during the prosecution of this application. To summarize briefly, Krivan teaches immunization of cattle to make antibodies to Shiga-like toxin. See, for example, col. 3-col. 4, col. 5, lines 42-50, and col. 8, lines 7-41. As noted at col. 8, lines 15-30, "the method of the invention is applied to any animal that has few or no receptors to

SLTs.", which thereby excludes humans. Krivan teaches that the use of polyvalent mixtures of antibodies is advantageous. Col. 5, lines 51-59. See also col. 19, lines 11-16 and figure 1. One should not confuse "monospecific" with monoclonal. This term is defined at col. 7, lines 51-56, as "the term "monospecific" refers to antibodies that do not have epitopes for antigens other than SLTs."

Krivan does say that his antibodies are useful to treat disorders caused by SLTs. See col. 10. The dosage range for non-human polyclonal antibodies is somewhere between 100 mg and 5 gram for treatment of an animal such as a pig, cow or human. Col. 10, lines 49-54. Col. 15-col. 16 describes making antibodies by injecting cows with SLT-II of unknown origin, other than E. coli, which could be a strain that does not infect humans or does not cause significant disease in human – there is no teaching that one should obtain antibodies that bind to the toxins produced by enteropathogenic *E. coli* causing HUS in humans. The claims, which the examiner has repeatedly referred to in support of his rejection, all refer to a "purified" SLT but does not define what "purified" means nor what the origin of the E. coli strain is that is the source of the SLT. Indeed, Krivan states at col. 7, line 65 to col. 8, line 6, that any SLT can be used. No method of isolating the SLT is provided, only a statement that known techniques can be used (see col. 8, lines 42-43) other than the very generalized method of example 1 at col 15, which provides no evidence that there all of the purified SLT-I was separated from the SLT-II (the use of an antibody reactive with one subunit, as shown by Perera, does not mean it is not also reactive with the other subunit). Absent a teaching to select a bacterial strain that causes enteropathogenic

disease in humans, as well as a teaching to purify the SLT subunit, and some teaching that indicates monoclonal antibodies are preferred to polyclonal antibodies, one simply cannot arrive at what appellants' claim. The importance of the selection of the toxin, as well as an animal model to confirm that the antibody will protect from disease in humans, is critical to what is claimed. (See, for example, Pradel, et al., Appl. Environ. Microbiol. 67(6), 2460-2468 (2001). There mere possibility that one could arrive at such a composition is not sufficient. The examiner has completely ignored this issue, presumably believing that any SLT II will work and any effective dosage can be derived, even in the absence of an appropriate animal model, asserting that the mere mention of using antibody to one of the various SLTs alone is sufficient motivation. This does not meet the legal standard.

Summary

The examiner has not made a novelty rejection but an obviousness rejection. However, it is not sufficient to identify references that potentially could be modified to arrive at what appellants' claim, unless there is some teaching to do so. This is not provided by Williams, Perera, or Krivan, alone or in combination.

The Dependent Claims

Appellants have presented evidence that different strains of E. coli infect different species, and induce different toxicity in different species. Indeed, this is the major argument that has been made repeatedly with respect to the need for the animal model discussed above – not only do the pigs contain the receptors for the toxins that are similar to humans, but the pigs are

infected with the same virulent strains that have the greatest mortality in humans. The discovery of this animal model is therefore essential to provide an effective amount of the human or humanized monoclonal antibodies to SLT II of *E. coli* which is enteropathogenic in humans. See, for example, declarations under 35 U.S.C. 132 of Dr. Saul Tzipori, dated April 10, 2003, and attached letters from Drs. Moon and Tarr; Dr. John M. Leong dated March 27, 2003, and Dr. Florian Gunzer dated April 1, 203.

The claims do not stand or fall together, as discussed in more detail below. There are a number of elements not disclosed by the prior art, in addition to the failure to provide the motivation to select and combine the elements as defined by the independent claims.

Claims 27-29 are drawn to the source of the monoclonal antibodies (claim 27, human; claim 28, recombinant DNA; claim 29, chimeric antibodies). As discussed above, the prior art does not describe or suggest the use of humanized monoclonal antibodies to prevent or treat HUS, just the opposite, teaching that polyclonal bovine or avian antibodies should work as therapeutics.

Claims 30 and 33 are specific to particular subunits of the Shiga like toxin II. As discussed above, the cited art teaches that it is SLTI (Williams) that is critical to disease, not that one can prevent or treat HUS using antibodies to only a single subunit of the toxin. This must be contrasted to disclosure relating to the production of antibodies to a specific subunit or portion thereof, which is useful in a neutralizing assay (Perera). A neutralizing assay is not the same as, nor predictive of, prevention or treatment of HUS in humans.

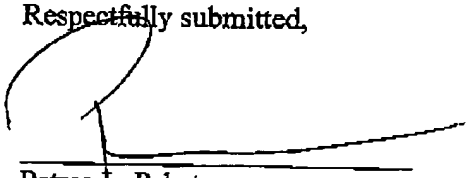
Claim 31 is drawn to a specific formulation for preventing the neurological signs of HUS - none of the prior art even recognizes this is an issue, much less provides guidance on what would be an effective amount to treat or prevent.

Claims 32, and 34- 36 relate to specific dosages. There is no art even remotely disclosing the effective dosages. First, none of the art states that one should use human or humanized monoclonal antibodies to prevent or treat HUS. Second, none teach that if one did have a preparation of such monoclonal antibodies, they should be administered in the claimed dosage ranges. Claim 32 is that amount prolonging survival. None of the art recognizes that the SLTII is critical to prevent or treat HUS, which is the leading cause of death in patients infected with enteropathogenic *E. coli*. Claim 34 defines a dosage of 4 ml serum/kg body weight. Williams provides a maximum of 1 ml/treatment, or less than 1 gram inpure protein and less than 100 mg pure protein. Krivan describes between 100 mg and 5 gram of inpure IgG administered orally, by injection, or topically (i.e., impossible to calculate). Claim 35 requires a dosage effective to produce a serum level of about 0.5 mg/ml – considerably more than the disclosure of Williams. Claim 36 requires a dosage of 3 mg antibody/baby piglet (approximately 1 kg; see Declaration of Dr. Saul Tzpori, signed April 10, 2003).

Serial No.: 10/041,958
Filed: January 7, 2002
REPLY TO EXAMINER'S ANSWER

For the foregoing reasons, Appellant submits that claims 26-36 are patentable.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: January 31, 2005

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151
(404) 879-2160 (Facsimile)

CP101cp 085337/4